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Case Report

Photodynamic Therapy to Control Life-Threatening Hemorrhage From Hereditary Hemorrhagic Telangiectasia

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Background and Objective: **Photodynamic therapy (PDT) was used to stop life-threatening hemoptysis from bleeding hereditary telangiectasia in bronchi in a 42-year-old man with a 4-year history of repeated embolotherapies, tracheostomies, and ventilator dependence. At the time of his first PDT, he was 10 days past his third embolotherapy, was being ventilated through a tracheostomy and bringing up 100–200 cc of blood daily, necessitating multiple transfusions of blood and platelets.**

Study Design/Material and Methods: **Four hours after intravenous injection (60 mg/m^2 body surface) of the photosensitizer dihematoporphyrin ether (DHE), bronchoscopy through his tracheostomy showed continuous oozing of non-clotting blood from bronchial vessels in both lung fields, requiring continuous suction. We performed PDT to seven bronchial sites. The 630 nm wavelength light energy to activate the photosensitizer was generated by a tunable dye argon laser system and delivered to the endobronchus through a quartz fiber modified with a 2.5 cm diffusing tip passed through the biopsy channel of the bronchoscope. The light power was 500 mW per cm of diffuser and the light dose was 200 J per cm of diffuser. At the end of the treatments, the bleeding had decreased so as not to require suctioning. The following day we treated three other sites with the same light dose. At this time the only bleeding was from the LUL, which oozed briskly after passing the bronchoscope through it. At the end of the treatment bronchoscopy there was minimal bleeding.**

Results: **One week after PDT he was discharged with a tracheosotomy and mechanical ventilator. Four months later his tracheostomy was removed. He remained free of hemoptysis for 26 months when life-threatening hemoptysis recurred. Twenty-two hours after his second injection of DHE, we treated four different endobronchial sites with PDT for bleeding from both the right and left bronchial tree. Sixteen months after his second PDT he remains free of hemoptysis. Three other patients treated for uncontrollable life-threatening hemoptysis from bronchitis have remained free of hemoptysis for 9, 17, and 23 months.**

Conclusions: **Photodynamic therapy causes thromobosis and can control bleeding from small vessels regardless of their location or etiology.**

Key words: photodynamic therapy, dihematoporphyrin ether, hereditary hemorrhagic telangiectasia

INTRODUCTION

Photodynamic therapy (PDT) destroys malignant tumors by using an intravenously injected photosensitizer that absorbs light energy and produces singlet oxygen. This causes thrombosis of tumor vessels and damage to the tumor cell wall and mitochondria [1,2].

During PDT to endobronchial tumors, we observed that bleeding decreased by the end of PDT[3]. At 283 consecutive PDT bronchoscopies, we recorded the amount of bleeding before, during, and at the end of PDT with a scale of 0 = none; 1 = mild (drops); 2 = moderate (controlled easily with suction); 3 = heavy (requiring tamponade); 4 = very heavy (life threatening). The mean bleeding scales at 24 bronchoscopies when there was bleeding of 2 or greater before PDT was 2.5 before PDT and 0.1 at the end of PDT ($P<.000$) [4]. We also observed bleeding from skin tumors stops at the end of, or shortly after, PDT and telangiectasias on the face in treated areas were not present after the skin healed [5].

These results lead us to use PDT to treat a patient with recurrent pulmonary hemorrhage from hereditary hemorrhagic telangiectasias.

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CASE REPORT

The past medical history of a 42-year-old white male with pulmonary arteriovenous malformations, hereditary hemorrhagic telangiectasia, and severe restrictive pulmonary disease from bilateral pleural thickening included recurrent bilateral chlyothoraces requiring multiple chest tubes. In December 1988, he developed life-threatening hemoptysis and had embolotherapy [6] to the left internal mammary and left bronchial arteries. His dyspnea increased after the embolotherapy.

In May 1989, he required emergency intubation and mechanical ventilation in the hospital for 61 days and was discharged with a tracheostomy and ventilator. Gradually his breathing improved enough to remove the tracheostomy.

Beginning in May 1991, repeated hospitalizations for respiratory arrest and failure resulted in a second tracheostomy and home ventilator. In August 1992, he had embolotherapy to the left internal mammary, left bronchial and left 6th intercostal arteries again for massive hemoptysis. Six weeks later he had embolotherapy to the right upper and lower bronchial and right 8th and 9 intercostal for recurrence. Ten days later he was admitted again with life-threatening hemoptysis.

On October 14, 1992, the patient was being ventilated through a tracheostomy, bringing up 100–200 cc of blood daily and requiring multiple transfusions of blood and platelets. Four hours after intravenous injection of 60 mg/m^2 body surface of the photosensitizer dihematoporphyrin ether (DHE; QuadraLogic Technologies, Vancouver, Canada), bronchoscopy through his tracheostomy showed continuous oozing (class 2) of nonclotting blood from bronchial vessels in both lung fields, requiring continuous suction. Most bleeding was from the left side. He also had numerous bilateral endobronchial pneumatoceles that expanded and partially obstructed the bronchi on respiration (Fig. 1).

We performed PDT to seven bronchial sites: left lower ledge bronchus (LLL), LLL segment 2, proximal left main bronchus (LMB), distal LMB, right main bronchus (RMB), right upper lobe bronchus (RUL), right middle lobe bronchus (RML). The 630 nm wavelength light energy to activate the photosensitizer was generated by a tunable dye argon laser system. This was delivered to the endobronchus through a quartz fiber modified with a 2.5 cm diffusing tip passed through the biopsy channel of the bronchoscope with a power of 500 mW and a dose of 200 J per cm of diffuser. At the end of the treatments, the bleeding had decreased so as not to require suctioning (class 1).

The following day we treated the LLL segment 1, LLL segment 3, and left upper lobe bronchus (LUL) with the same light dose. At this time there was no bleeding except for the LUL, which oozed briskly (class 2) after passing the bronchoscope through it. At the end of the treatment bronchoscopy there was minimal bleeding (class 1).

One week after PDT he was discharged with a tracheosotomy and mechanical ventilator. Four months later his tracheostomy was removed. He remained free of hemoptysis, but in November 1994, he required his third tracheostomy for mechanical ventilation.

On December 20, 1994 (26 months after his first PDT), he was readmitted with recurrence of life-threatening themoptysis. Twenty-two hours after his second injection of dihematoporphyrin ether (DHE), we treated the RMB, RUL, R (right) posterior segment, and LMB with PDT for class 2 bleeding from both the right and left bronchial trees. The pneumatoceles seen in 1992 were absent except for a 1 mm bleb on the RMB. At the end of the bronchoscopy, there was no bleeding.

One day later we rebronchoscoped him and treated the right anterior and posterior segments 1 and 2 for class 2 bleeding. There was no bleeding at the end of bronchoscopy. Bronchoscopy the next day showed no bleeding and the small bleb on the RMB was not present. Four days after PDT he was discharged home with a tracheostomy and ventilator. Sixteen months after this PDT, he has had no hemoptysis since his discharge, is ambulatory during the day, and uses the ventilator only at night.

DISCUSSION

Photodynamic therapy causes thrombosis and can control bleeding from small vessels regardless of their location or etiology. We have used photodynamic therapy to stop bleeding from malignant endobronchial lesions. Some of these patients had massive hemoptysis, were on a respirator, or were confined to bed with prospects of imminent asphyxia.

In addition to this patient with hereditary hemorrhagic telangiectasias, three patients with uncontrollable life-threatening hemoptysis from bronchitis were also successfully treated with

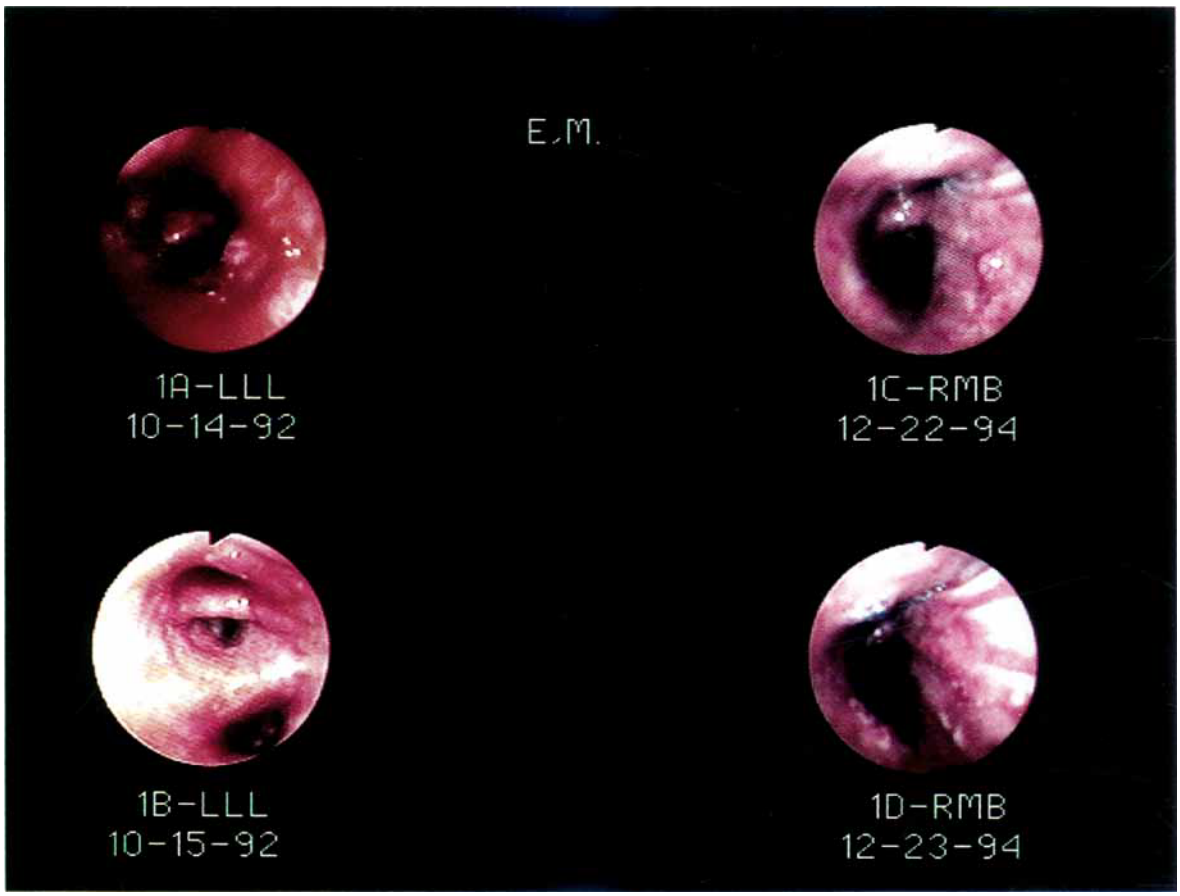

Fig. 1. **(A)** shows pneumatoceles and bleeding from the LLL before photodynamic therapy (PDT). **(B)** shows cessation of bleeding one day after PDT. **(C)** shows a small pneumatocele in RMB 26 months after first PDT. **(D)** shows obliteration of pneumatocele 1 day after PDT.

PDT. A 72-year-old female at bed rest with continuous oxygen was coughing large blood clots. Seventeen months after PDT, she has no hemoptysis or dyspnea and has been working for the last 15 months. A 65-year-old male with COPD has had no recurrence of hemoptysis for 23 months. A 78-year-old male has had no recurrence of hemoptysis 9 months after PDT to the lingula for massive hemoptysis.

It has been brought to our attention that many of these patients present with epitaxis that is uncontrollable, and certainly photodynamic therapy would present an option for these patients.

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